

# Appendectomy Should Be Performed During Minimally Invasive Surgery for Endometriosis

Ariella Farzan Nikou, BS, Nicole Sara Tenzel, MD, Peiyong Hua, MS, Laurence Orbuch, MD, Iris Kerin Orbuch, MD

## ABSTRACT

**Objectives:** To determine the prevalence of appendiceal histopathology in patients with confirmed endometriosis following minimally invasive surgery (MIS) for endometriosis. To determine whether pre-operative symptoms, age, intra-operative appendiceal appearance, or endometrioma laterality were associated with appendix histopathology in patients with suspected endometriosis.

**Methods:** One hundred thirty-five patients ages 16–52 with suspected endometriosis undergoing MIS for endometriosis with concomitant appendectomy at two metropolitan academic hospitals from January 1, 2012 to June 30, 2017 were included in this retrospective chart-review study. Medical records were reviewed for pre-operative symptoms, age, intraoperative appendix appearance, appendix histopathology, histopathologically-confirmed endometriosis, and endometriomas.

**Results:** In patients with confirmed endometriosis, the prevalence of all appendiceal histopathology was 25%, which included appendiceal endometriosis (18%), appendiceal tumors (2%), and inflammation (5%). Dyspareunia was

the only pre-operative symptom significantly associated with appendiceal histopathology ( $p=0.04$ ). The presence of a right endometrioma was associated with appendiceal histopathology ( $p=0.009$ ). Additionally, appendiceal histopathology was not significantly associated with age nor intra-operative appendiceal characteristics.

**Conclusion:** This manuscript adds to the limited pool of studies regarding appendiceal histopathology and appendiceal tumors in patients with suspected and confirmed endometriosis. On the basis of the high rate of histopathological appendices found in this population; the lack of association with possible diagnostic factors such as age, most pre-operative symptoms, and intra-operative appendiceal characteristics; and the relatively low risks of concomitant appendectomy, we suggest that surgeons consider concomitant appendectomies at the time of MIS for endometriosis.

**Key Words:** Appendectomy, Endometrioma, Endometriosis, Tumor.

Icahn School of Medicine at Mt Sinai, New York, NY (Dr Nikou).

Obstetrics, Gynecology, and Reproductive Science, Mt Sinai Health System, New York, NY (Drs Tenzel, Laurence Orbuch and Iris Kerin Orbuch).

Population Health Science and Policy, Icahn School of Medicine at Mt Sinai, New York, NY (Dr Hua).

Advanced Gynecologic Laparoscopy Center of Los Angeles and New York City, Beverly Hills, CA (Drs Laurence Orbuch and Iris Kerin Orbuch).

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Address correspondence to: Ariella Farzan Nikou, BS, Icahn School of Medicine at Mount Sinai, New York, NY, Telephone: 310-850-0051, E-mail: ariella.farzannikou@icahn.mssm.edu

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## INTRODUCTION

The benefits of concomitant appendectomy at the time of minimally invasive surgery (MIS) for endometriosis have been the subject of debate. Some cited benefits of concomitant appendectomy include preventing future emergency appendectomies and excluding appendicitis in patients with endometriosis.<sup>1</sup> Appendectomies have low rates of complications and there are multiple minimally invasive methods to perform them.<sup>1–3</sup> Currently the American College of Obstetricians and Gynecologists (ACOG) suggests that concomitant appendectomies are most beneficial for women younger than 35 years after taking into account the incidence and risks of appendicitis. Concomitant appendectomy is also beneficial for patients due to the increased incidence of appendiceal endometriosis, tumors, and other forms of appendiceal histopathology, which are frequently visually undetectable during surgery.<sup>4–6</sup>

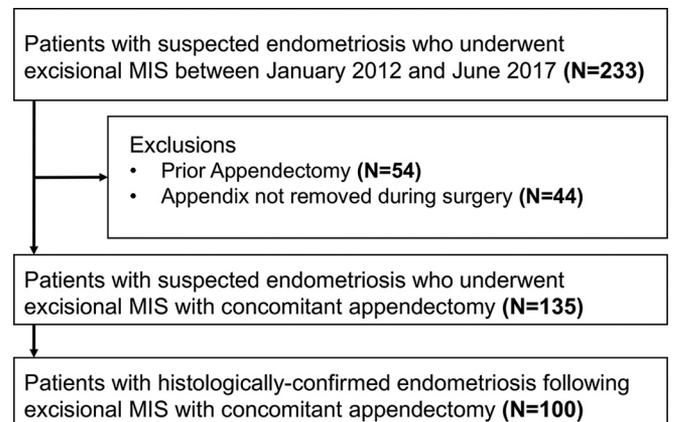
The reported prevalence of appendiceal endometriosis ranges between 2.6–13.2%.<sup>4-9</sup> The prevalence of appendiceal tumors is understudied, especially in women with endometriosis. The reported prevalence of appendiceal tumors in the general population, usually diagnosed incidentally, ranges between 0.16–2.3%.<sup>10</sup> In patients who underwent gynecological procedures, the prevalence of appendiceal tumors is higher and ranges between 0.75–2.6%.<sup>5,11</sup>

The objective of this study is to address the role of concomitant appendectomy in patients with suspected or known endometriosis who underwent MIS by reporting the prevalence of appendiceal histopathologies (i.e., endometriosis, tumors, acute or chronic inflammation) in these patients and investigating the association of age, pre-operative symptoms, intraoperative appendiceal characteristics, and the presence of endometriomas in patients with suspected endometriosis.

## MATERIALS and METHODS

This study was reviewed and approved by the Institutional Review Board of our institution and was determined to be exempt from human research. The study population for this retrospective chart review included patients with suspected endometriosis who underwent MIS of endometriosis with concomitant appendectomy between January 1, 2012 and June 30, 2017. A total of 233 patients were identified for this study by searching medical records for current procedural terminology codes related to endometriosis and appendectomy performed by the authors of this study. Patients were excluded if they had a prior appendectomy ( $n = 54$ ) or if their appendix was not removed during surgery ( $n = 44$ ) (**Figure 1**). All patients without a history of prior appendectomy were counseled on concomitant appendectomy during their pre-operative appointment. 24.6% (44/179) of patients elected not to have their appendix removed if a normal appearing appendix was visualized during surgery. A total of 135 patients with suspected endometriosis between the ages of 16–52 who underwent MIS of endometriosis and concomitant appendectomy were included. A subgroup of 100 patients aged 16–51 were histopathologically diagnosed with endometriosis (at least one positive biopsy) following MIS for suspected endometriosis and concomitant appendectomy (**Figure 1**).

The following data was abstracted from the medical record, operative report, and pathology report for every patient: age; pre-operative symptoms (i.e. dysmenorrhea,



**Figure 1.** Study cohort flow diagram.

dyspareunia, dyschezia, menorrhagia, dysuria/frequency, right lower quadrant pain, left lower quadrant pain, constipation, diarrhea, nausea, back pain, ovarian cyst); intra-operative appendiceal characteristics (i.e. thickening, scarring/adhesions, discoloration, nodularity, vascular congestion, irregular shape); the presence of appendiceal histopathology (i.e. endometriosis, tumor, acute or chronic inflammation); histopathological evidence of endometriosis on at least one biopsy; and the presence of endometriomas and their respective laterality. The deidentified data was stored in an electronic database for statistical analysis.

The prevalence of appendiceal histopathologies and corresponding 95% confidence intervals (CI) were calculated (i.e. endometriosis, tumors, acute or chronic inflammation) for confirmed endometriosis patients. Association between age, intra-operative appendix appearance, and pre-operative symptoms with appendiceal histopathology was performed using T-test, Pearson  $\chi^2$  test, or Fisher's Exact test, as appropriate. Dyschezia, constipation, diarrhea, and nausea were grouped together as gastrointestinal symptoms. The prevalence of bilateral endometrioma (BE), right endometrioma (RE), left endometrioma (LE), and absence of any endometrioma (AE) were calculated. Pearson  $\chi^2$  test and Fisher's Exact test were used to determine the association between laterality of endometrioma and appendiceal histopathology. Values of  $P < .05$  were considered statistically significant.

## RESULTS

The mean age of all 135 patients undergoing MIS of endometriosis with concomitant appendectomy for

suspected endometriosis was  $32.4 \pm 7.6$  years. Patients with and without appendiceal histopathology (i.e. endometriosis, tumor, chronic/acute inflammation) had mean ages of  $33.4 \pm 8.6$  and  $31.8 \pm 6.9$  years, respectively, with no significant difference ( $P = .25$ ). Similarly, there was no significant difference in the rates of appendiceal histopathology between age groups ( $\leq 35$  vs.  $>35$ ) ( $P = .24$ ). Patients with and without endometriosis had mean ages of  $33.5 \pm 7.6$  and  $32.3 \pm 7.6$  years, respectively. Patients with and without appendiceal tumors had mean ages of  $26.8 \pm 7.1$  and  $32.6 \pm 7.6$  years, respectively (**Table 1**).

In patients with confirmed endometriosis, 25% (95% CI: 16.5–33.5%) had underlying appendiceal histopathology with the following breakdown: 18% (95% CI: 10.5–25.5%) with endometriosis, 5% (95% CI: 0.7–9.3%) with acute or chronic inflammation, and 2% (95% CI: 0–4.7%) with appendiceal tumors (**Table 2**). In our cohort, we also found a prevalence of 17.0% (95% CI: 9.6–24.4%) for fibrous obliteration.

Pre-operative symptoms and intra-operative appendiceal characteristics were investigated to determine if they were associated with the presence of appendiceal histopathology. Dyspareunia was the only pre-operative symptom that was significantly associated with appendiceal histopathology compared to those with normal histopathology (81.5% vs. 65.4%;  $P = .04$ ). Gastrointestinal symptoms (i.e. dyschezia, constipation, nausea, and diarrhea), dysmenorrhea, menorrhagia, dysuria, right lower quadrant pain, left lower quadrant pain, back pain, and presence of ovarian cyst were not significantly associated with appendiceal histopathology (**Table 3**). Likewise, intra-operative appendiceal characteristics such as thickening, scarring/adhesions, discoloration, nodularity, vascular congestion, or irregular shape of the appendix were not significantly associated with underlying appendiceal histopathology (**Table 4**).

The relationship between endometriomas and appendiceal histopathology was also explored. Of the 135 patients with suspected endometriosis, 79.3% were in absence of AE, 5.9% had RE only, 5.9% had LE only, and 8.9% had BE (**Figure 2**). Eighty-eight percent of patients with a RE had appendiceal histopathology. The presence of a RE vs. AE was associated with the presence of appendiceal histopathology (87.5% vs. 38.3%;  $p = .009$ ). The presence of a RE vs. LE was not associated with appendiceal histopathology (87.5% vs. 50%;  $p = .28$ ).

Of the patients with suspected endometriosis, 4 (3%) patients had appendiceal tumors. Of these cases, three

**Table 1.**  
Mean Ages of Patient Groups with Suspected Endometriosis

Patients	Mean Age (Years) $\pm$ SD	p-Value
All Patients	$32.4 \pm 7.6$	NA
Appendiceal Histopathology Negative	$31.8 \pm 6.9$	0.25
Appendiceal Histopathology Positive	$33.4 \pm 8.6$	
Endometriosis Negative	$32.3 \pm 7.6$	NC
Endometriosis Positive	$33.5 \pm 7.6$	
Tumor Negative	$32.6 \pm 7.6$	NC
Tumor Positive	$26.8 \pm 7.1$	

NC, not calculated; NA, not applicable.

**Table 2.**  
Prevalence of Appendiceal Histopathology in Patients with Endometriosis

Appendiceal Histopathology	Prevalence (n = 100) (95% Confidence Interval)
Endometriosis	18.0% (10.5 – 25.5%)
Tumor	2.0% (0.0 – 4.7%)
Acute/Chronic Inflammation	5.0% (0.7 – 9.3%)
All Appendiceal Pathologies	25.0% (16.5 – 33.5%)

were well-differentiated neuroendocrine carcinoid tumors (0.5 cm, 0.6 cm, and 10.1 cm respectively) that invaded the muscularis propria, subserosal tissue, and mesoappendix; and one was a low grade appendiceal mucinous neoplasm (LAMN) (**Table 5, Figure 3**). The neuroendocrine and carcinoid biomarkers synaptophysin and chromogranin-A were expressed in two of the carcinoid tumors.<sup>12,13</sup> All three were found in the distal appendix with two of them in the appendiceal tip and all of the resected margins were free of the tumor. Postappendectomy, two of the patients with carcinoid tumors required no further treatment, but one underwent a right hemicolectomy after the initial surgery. The LAMN tumor was confined to the appendix and the resected margin was free of the tumor. Two of the four patients with appendiceal tumors had histopathologically-confirmed endometriosis, a patient with the 0.6 cm carcinoid and another with a LAMN (**Table 5**). The four tumors found in patients with suspected endometriosis were grossly abnormal in appearance.

**Table 3.**  
Pre-operative Symptoms and Appendiceal Histopathology in Patients with Suspected Endometriosis

Preoperative Symptom	Normal (n = 81)	Appendiceal Histopathology (n = 54)	p-Value
Gastrointestinal Symptom*			0.31
No	26/81 (32.1%)	13/54 (24.1%)	-
Yes	55/81 (67.9%)	41/54 (75.9%)	-
Dysmenorrhea			1.00
No	2/81 (2.5%)	2/54 (3.7%)	-
Yes	79/81 (97.5%)	52/54 (96.3%)	-
Dyspareunia			<b>0.04</b>
No	28/81 (34.6%)	10/54 (18.5%)	-
Yes	53/81 (65.4%)	44/54 (81.5%)	-
Menorrhagia			0.74
No	72/81 (88.9%)	47/54 (87.0%)	-
Yes	9/81 (11.1%)	7/54 (13.0%)	-
Dysuria			0.60
No	56/81 (69.1%)	35/54 (64.8%)	-
Yes	25/81 (30.9%)	19/54 (35.2%)	-
Right Lower Quadrant Pain			0.74
No	61/81 (75.3%)	42/54 (77.8%)	-
Yes	20/81 (24.7%)	12/54 (22.2%)	-
Lower Left Quadrant Pain			0.93
No	64/81 (79.0%)	43/54 (79.6%)	-
Yes	17/81 (21.0%)	11/54 (20.4%)	-
Back Pain			0.12
No	71/81 (87.7%)	52/54 (96.3%)	-
Yes	10/81 (12.4%)	2/54 (3.7%)	-
Ovarian Cyst			0.67
No	64/81 (79.0%)	41/54 (75.9%)	-
Yes	17/81 (21.0%)	13/54 (24.1%)	-

\*Includes dyschezia, constipation, nausea and diarrhea.

There were no minor or major complications from the concomitant appendectomies that were performed.

## DISCUSSION

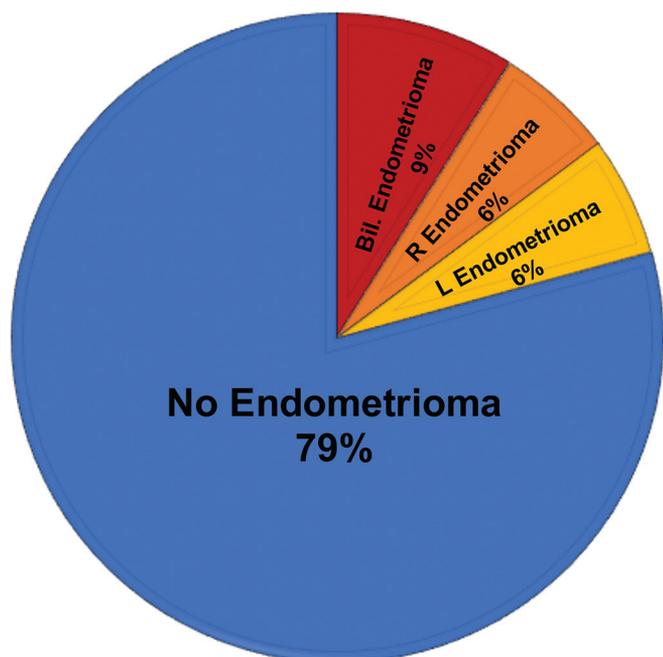
ACOG recommends concomitant appendectomy in patients younger than 35 (based on the risk of appendicitis, but not other appendiceal pathologies), but we found that the rates of appendiceal histopathology were similar between age groups  $\leq 35$  and  $\geq 35$  (36.4% vs. 46.8%).<sup>1,14</sup>

This study and others have shown that there was no difference in mean age between patients with and without appendiceal endometriosis.<sup>6</sup> Additionally, the mean age of the patients with appendiceal tumors in this study is consistent with the finding that the incidence of carcinoid tumors peaks in the 20–39 age demographic,<sup>15</sup> but is much younger than 57 years, the median reported age of appendiceal tumors in the literature.<sup>11,16–18</sup>

Our study found a higher prevalence of appendiceal endometriosis in confirmed endometriosis patients than other studies (18% vs. 12–13.2%), which may be due to

**Table 4.**  
Intra-operative Appendiceal Characteristics and Appendiceal Histopathology in Patients with Suspected Endometriosis

Intraoperative Appendiceal Characteristics	Normal (n = 81)	Appendiceal Histopathology (n = 54)	p-Value
Thickening			1.00
No	36/81 (44.4%)	24/54 (44.4%)	-
Yes	45/81 (55.6%)	30/54 (55.6%)	-
Scarring/Adhesions			0.23
No	40/81 (49.4%)	21/54 (38.9%)	-
Yes	41/81 (50.6%)	33/54 (61.1%)	-
Discoloration			0.62
No	68/81 (84.0%)	47/54 (87.0%)	-
Yes	13/81 (16.1%)	7/54 (13.0%)	-
Nodularity			0.48
No	60/81 (74.1%)	37/54 (68.5%)	-
Yes	21/81 (25.9%)	17/54 (31.5%)	-
Vascular Congestion			0.49
No	62/81 (76.5%)	44/54 (81.5%)	-
Yes	19/81 (23.5%)	10/54 (18.5%)	-
Irregular Shape			0.77
No	69/81 (85.2%)	45/54 (83.3%)	-
Yes	12/81 (14.8%)	9/54 (16.7%)	-



**Figure 2.** Prevalence of endometriomas in patients with suspected endometriosis.

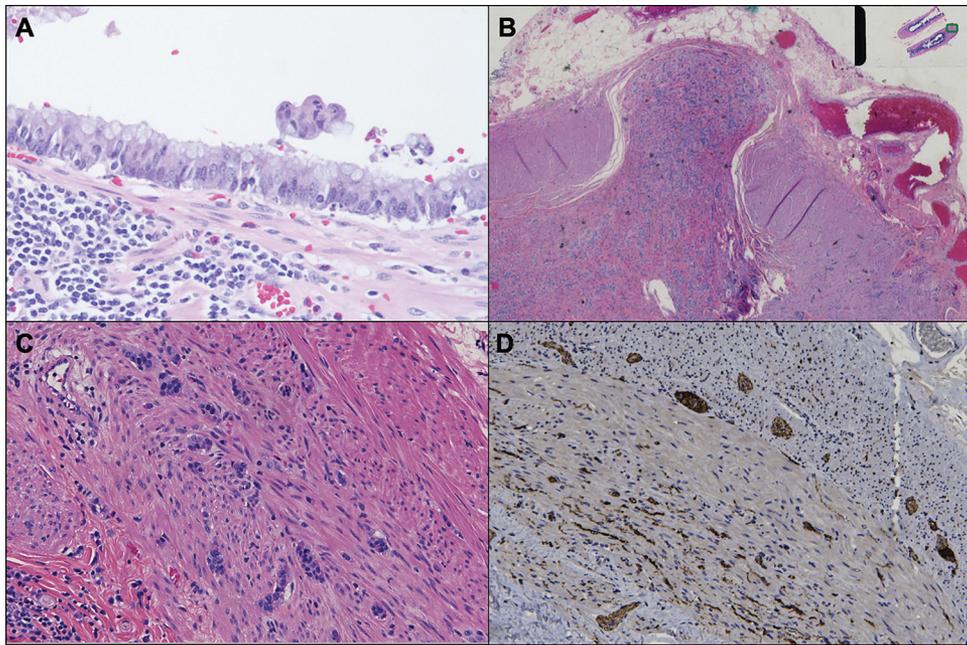
the fact that out of 179 patients who possessed an appendix at the time of surgery, a high proportion, 135 (75.4%), underwent appendectomy.<sup>5-7</sup> Of note we found a 17% prevalence of fibrous obliteration in our cohort, which is not included in the total prevalence of appendiceal pathology due to its indeterminate clinical significance. Our study is consistent with other studies which found that the rate of appendiceal histopathology far exceeds abnormal visual cues during surgery.<sup>4-6</sup> Thus our data indicates that a visually normal appendix may in fact be pathologically abnormal.

Dyspareunia was the only pre-operative symptom that was significantly associated with appendiceal histopathology in this study, which may be due to rectovaginal septum or cul-de-sac endometriosis, which then travels to the appendix via the clockwise flow of peritoneal fluid.<sup>9,19</sup> Mabrouk et al. found that patients with appendiceal endometriosis reported significantly higher rates of severe dyschezia, constipation, and pain in the right iliac fossa, but these results were not replicated in our study.<sup>9</sup>

Our study's finding that REs are associated with appendiceal histopathology is consistent with another recent study that REs are an independent risk factor for

**Table 5.**  
Tumor Characteristics in Patients with Suspected Endometriosis

Tumor	Age (Years)	Nearby Tissue Invasion	Other Characteristics
0.5 cm Carcinoid	17	Muscularis Propria	Right hemicolectomy; Synaptophysin +
0.6 cm Carcinoid	32	Subserosal Tissue	Confirmed Endometriosis
1.1 cm Carcinoid	26	Mesoappendix	Chromogranin-A and Synaptophysin +
Low-grade Appendiceal Mucinous Neoplasm	32	None: confined to appendix	Confirmed Endometriosis



**Figure 3.** A) Low grade appendiceal mucinous neoplasm with elongated dysplastic cells, apical mucin (200x) B) 0.6 cm well-differentiated carcinoid invading the subserosal tissue (25x) C) 0.5 cm well-differentiated carcinoid with nests/cords of neoplastic cells (200x) D) 0.5 cm well-differentiated carcinoid with synaptophysin stain (100x).

appendiceal endometriosis.<sup>9</sup> The relationship between REs and appendiceal endometriosis has been proposed to be due to the physical colocalization of the right ovary and appendix; and that the left adnexa is shielded from the right adnexa by the sigmoid colon, which frequently adheres to the pelvic brim forming a segregated area for the left adnexa.<sup>9,19</sup> Thus, endometriosis implants in the left side of pelvis may not be able to easily infiltrate the clockwise peritoneal flow of fluid and move to the appendix on the right side of the pelvis.<sup>9,19</sup> There would be no such hindrance for endometriosis from the right adnexa. The relationship between RE and appendiceal histopathology in general requires further study.

Furthermore, the prevalence of appendiceal tumors in patients with confirmed endometriosis in our study is consistent with the prevalence rate of appendiceal tumors reported in the literature (2% vs. 0.16–2.3%).<sup>10</sup> Interestingly, the two additional appendiceal tumors found in patients who did not have biopsy-confirmed endometriosis had suspected adenomyosis at the time of surgery. The most common tumor found in our cohort was appendiceal carcinoid tumors which is the most common appendiceal tumor.<sup>10</sup> Carcinoid tumors cause symptoms when the tumor becomes metastatic, approximately 9 years on average, so it is beneficial for these tumors to be excised early in their development as was the case in our cohort where the tumors were small and did not

extend past the resection margin.<sup>10,20</sup> An appendectomy is usually sufficient to treat a carcinoid tumor that has no evidence of metastasis and right hemicolectomy is usually considered when the tumor is  $\geq 2$  cm in diameter, which only occurred in one of our patients.<sup>15,16</sup> One of the tumors in our cohort was an LAMN, a tumor that can be complicated by pseudomyxoma peritonei which is associated with a 45% survival rate over 10 years; this complication had fortunately not developed in our patient.<sup>17,21,22</sup>

There is also evidence that appendectomies are beneficial for the treatment of chronic pelvic pain (CPP) due to appendiceal pathologies or even when no pathology is determined. A study showed that 89% of women who had inconclusive laparoscopies for CPP had evidence of a pathological appendix, thus appendiceal pathologies may be an important cause of CPP.<sup>7</sup> Additionally, 91% of women suffering from CPP reported a decrease in their pain after an appendectomy, the main surgical intervention.<sup>4</sup> Furthermore, 31% of these patients had improvement in their pain with an appendectomy, though there was no evidence of appendiceal pathology.<sup>4</sup> Another study found a significant decrease in CPP in the appendectomy group vs, nonappendectomy group after 6 weeks, despite only an 11% pathological appendix rate in the appendectomy group.<sup>23</sup>

This study has several strengths. This study is a multicenter preliminary study exploring the understudied role of appendiceal histopathology in patients with suspected and confirmed endometriosis. In addition to describing the prevalence of appendiceal endometriosis, this study also specifically focused on the heretofore underexplored prevalence of appendiceal tumors in this population. Furthermore, this study investigated the associations between appendiceal histopathology and a host of diagnostic parameters such as pre-operative symptoms, age, intra-operative appendiceal appearance, or endometrioma laterality to help develop guidelines for appendectomy in these patients. Some limitations should be acknowledged. This study has a relatively small sample size, is retrospective in nature, and does not include a control group. However, it lays the groundwork for a future prospective randomized trial.

## CONCLUSION

In summary, we found a high prevalence of appendiceal endometriosis (18%), appendiceal tumors (2%), and appendiceal pathology (25%) in patients with confirmed endometriosis. In light of this high prevalence

and the lack of association with age, pre-operative symptoms (other than dyspareunia), or abnormal intra-operative visual appendiceal characteristics; pre-operative and intraoperative decision making will miss many pathologically abnormal appendices. This data along with the low morbidity associated with concomitant appendectomy suggests that all surgeons should consider routine concomitant appendectomy. Further larger studies are necessary.

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